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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,245	11/15/2001	Jens Holm	4305/1H942-US2	9286

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DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
07/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/001,245	HOLM ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,35,37-39 and 66-85* is/are pending in the application.

4a) Of the above claim(s) *16 and 18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 17, 35, 37-39 and 66-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 04/07/2009 is acknowledged.

2. Claims 1-22, 35, 37-39 and 66-85 are pending.

3. Claims 16 and 18-22 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/09/2008.

4. Claims 1-15, 17, 35, 37-39 and 66-85 are currently pending and under consideration as they read on the recombinant mutant Der p 2 allergen with the mutations K15E S24N H30G K48A E62S K77N K82N and K100N of SEQ ID NO:36.

5. In view of Applicant's amendment and response filed on 04/07/2009, only the following rejections are maintained.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-15, 35, 37-39 and 66-85 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-96 of copending Application No. 10/719,553. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims arrive at similar allergenic variants, and by what appears to the Examiner by the same method of selection, or if not by an obvious variant thereof. Specifically, Claims 36-96 of the '553 Application teach a mutant Bet V 1 allergen with 1 or more substitutions, wherein said substitutions occur at many amino acid residues that are identical between the '553 application and the instant application, such as those recited in copending claim 37 and instant claim 22.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's argument filed on 04/07/2009 has been fully considered, but is not found persuasive.

Applicant acknowledges this provisional rejection and asks that it be held in abeyance.

The rejection is maintained until a terminal disclaimer is filed or the conflicting claims are cancelled or amended.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-15, 17, 35, 37-39 and 66-85 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons as set forth in the Office Action mailed on 10/07/2008.

Applicant's arguments filed on 04/07/2009 have been fully considered, but are not found persuasive.

Applicant argues:

> "The written description should be withdrawn because the Examiner has failed to state facts that establish a lack of written description. The Examiner first stated basis for lack of written description is that the specification does not disclose a correlation between the structure of the claimed allergens and function. *See* Office Action at page 7. The Examiner asserts that a large number of features set out in the claims are functional limitations. Office Action at pages 8 through 13, bold type. The Examiner's assertion is not correct. Features such as spacing between point mutations, surface exposure of amino acids, sequence identity among proteins, and spacing of mutations such that a circular region of at least 800 A^2 comprises no mutation are not "functional limitations." These are physical features that are describe the amino acids that are mutated in the recombinant mutant allergens and how they are placed. No "function" is explicitly recited or inherently present in these terms. It is thus error for the Examiner to base the present written description rejection, either in whole or in part, on the assertion that there is no correlation of structure to these "functional limitations."
>
> The Examiner is correct to characterize "reduced IgE binding" as a functional limitation. The specification, however, provides a straight forward disclosure that amino acids to be substituted to reduce

IgE binding are preferably located on the surface of an allergen, having a solvent accessibility of at least 20%,and are preferably located in a conserved patch having an area larger than 400 A^2. This is ample disclosure to show the inventors were in possession of mutations that reduce IgE binding.

The disclosure required to satisfy the written description requirement is measured against the background knowledge in the field. Considering factors for considering genus claims to genetic inventions set out by the Federal Circuit in Capon and Carnegie Mellon, here, the state of knowledge in the filed of allergens was high, both for identifying IgE epitopes and the structural knowledge of the families of allergens recited in the claims, the technology for making allergen mutants and identifying mutations that reduced IgE binding was high, and it was predictable that mutations made according to the guidance set out in the specification would reduce IgE binding. In short, when "applied in the context of the particular invention and the state of the knowledge" *(Capon v. Eshhar,* 418 F.3d at 1357), the specification provides ample disclosure to show the inventors had possession of mutations that "reduced IgE binding."

For at least the reasons set out above, the written description rejections asserted on the basis of "functional limitations" should be withdrawn.

With regard to the specific rejection of composition claims set out in the Office Action in the middle of page 13, the specification discloses recombinant mutant allergens, explicitly provides that such allergens may be formulated in compositions, and that such compositions may comprise the precise number of recombinant mutant allergen variants called for in the claims. The specification thus provide explicit support for the composition claims. The Examiner has failed to provide a single fact that supports the conclusion that the specification fails to provide written description for these claims. The written description rejection as it pertains to the composition claims should thus be withdrawn."

The specification does not adequately describe the correlation between the amino acid sequence of the recombinant mutant allergens encompassed by the instant claim limitations and the resulting function of reduced specific IgE binding capability. The allergens encompassed by the instant claim recitations include natively folded allergens, denatured allergens and fold variants. There is inadequate written description in the specification to describe the genus of allergen mutants where the mutations to surface exposed amino acids residues are at least 15 angstroms apart. In a denatured allergen, as encompassed by the instant claim recitations, all amino acids are surface exposed and given that amino acid residues are approximately 1.5 angstroms wide, then allergens with mutations at least 10 amino acids apart are encompassed. The specification does not adequately describe which of these allergens with exhibit reduced IgE binding. Further, there is inadequate written description for the genus of mutant allergens with at

least four mutations that have at least one circular surface region with a area of 800 angstroms that comprises no mutation. The limitation of "a circular surface region" without mutation lends very little to the claims as the claims do not require that the protein be folded in any particular manner. The amino acid sequence may be linear or randomly associated without disulfide bonds with a circular surface region without mutation. There is no correlation between those allergen mutants encompassed and reduced IgE binding.

It is the Examiner's position that the structure of a polypeptide allergen refers to its amino acid sequence. The way the protein folds, the distance between amino acids in a folded protein, the surface regions without mutation and other characteristics recited in the claims are all variables based how the protein is folded. Since the claims do not recite that they allergens need to be folded in any particular manner, determining which allergens are encompassed by the instant claim recitations is unpredictable. Because the specification does not disclose a correlation between the structure of the claimed recombinant allergens (complete combinations of specific mutations to a reference sequence) and function (which each reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen), a skilled artisan would not have known what modifications to make to the allergens to attain the claimed function. "Possession may not be shown by merely describing how to obtain possession of member of the claimed genus or how to identify their common structural features" *Ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)), at page 16. The instant claims encompass a genus of allergens that comprise mutations that are claimed based on spacing. The specification has described only the specific recombinant mutants of Ves v 5, Bet v 1, Der p 2, Der p 1 and Phl p 5 in Examples 1-10. Applicants have not provided

sufficient guidance as to what mutation or combination of mutations will result in the claimed function. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra*, at page 17.

It is also remains the Examiner's position that the specification also has also not adequately described the genus of compositions "comprising two or more recombinant mutant allergens" of claim 37: comprising 2-12 recombinant mutant allergens" of claim 38; "comprising 3-10 recombinant mutant allergens" of claim 84; or "comprising 5-7 recombinant mutant allergens" of claim 85 for use in the claimed invention. Claims 35 and 39 recite compositions comprising pharmaceutically acceptable carrier, excipient or adjuvant, but the specification has not adequately described the genus of mutant allergens that can be used in a pharmaceutical composition. Contrary to Applicant's assertion there is not explicit support in the specification for the genus of allergens mutant compositions encompassed or for pharmaceutical use.

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 2, 2009
Nora M. Rooney
Patent Examiner
Technology Center 1600

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644